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Domesticated animals and human infectious diseases of zoonotic origins: Domestication time matters

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ABSTRACT

The rate of emergence for emerging infectious diseases has increased dramatically over the last century, and research findings have implicated wildlife as an importance source of novel pathogens. However, the role played by domestic animals as amplifiers of pathogens emerging from the wild could also be significant, influencing the human infectious disease transmission cycle. The impact of domestic hosts on human disease emergence should therefore be ascertained. Here, using three independent datasets we showed positive relationships between the time since domestication of the major domesticated mammals and the total number of parasites or infectious diseases they shared with humans. We used network analysis, to better visualize the overall interactions between humans and domestic animals (and amongst animals) and estimate which hosts are potential sources of parasites/pathogens for humans (and for all other hosts) by investigating the network architecture. We used centrality, a measure of the connection amongst each host species (humans and domestic animals) in the network, through the sharing of parasites/pathogens, where a central host (i.e. high value of centrality) is the one that is infected by many parasites/pathogens that infect many other hosts in the network. We showed that domesticated hosts that were associated a long time ago with humans are also the central ones in the network and those that favor parasites/pathogens transmission not only to humans but also to all other domesticated animals. These results urge further investigation of the diversity and origin of the infectious diseases of domesticated animals in their domestication centres and the dispersal routes associated with human activities. Such work may help us to better understand how domesticated animals have bridged the epidemiological gap between humans and wildlife.

1. Introduction

Amongst the species listed as human pathogens 60 per cent are presented as zonootic (Cleaveland et al., 2001; Woolhouse and Gowtage-Sequeria, 2005). How parasite/pathogen communities of humans have been built-up in time and space has been the aim of several historical, ecological and evolutionarily studies (McNeill, 1976; Wolfe et al., 2007; Dunn et al., 2010; Gómez et al., 2013), with the assumptions that revealing the past may help to understand the present and infer future trends. Reviews emphasize that humans have gained their parasites and infectious agents either through descent (i.e. inherited from a common ancestor) or by acquiring them from either wild or domesticated animal species according to three major hypotheses (Wolfe et al., 2007; Perrin et al., 2010; Morand, 2012): the "out of Africa" source where parasites followed the dispersal and expansion of modern humans in and out of Africa; the "domestication" source where parasites were captured in domestication centres and then dispersed more widely; and the "globalization" source, which reflects the distribution of parasites in relation to historical and more recent trade routes.

The role played by domestic animals in the building of human parasite/pathogen diversity was hypothesized a long time ago by McNeill (1976), who was the first to suggest a positive relationship (although not statistically tested) between the number of parasite species shared between domesticated animals and humans and the length of time since their domestication. Here, we reinvestigated

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the hypothesis of McNeill using several other data sources and more accurate information on the dates and origins of domestication (Driscoll et al., 2009). We aimed, first, to confirm statistically the relationship hypothesized by the environmental historian McNeill (1976).

Second, and in order to better explore the potential mechanisms underlying the observed relationship between parasites/pathogens shared and time since domestication, we used network analysis. Network-based approaches have been widely used in epidemiology and disease ecology to study transmission heterogeneity (Bansal et al., 2007) in particular, how network topology may determine pathogen transmission across human and wildlife populations (Salathé and Kazandjieva, 2010; Gómez et al. 2013). By using network analysis, we aimed to (1) better visualize the overall interactions between humans and domestic animals (and amongst animals) and (2) estimate which hosts are potential sources of parasites/pathogens for humans (and for all other hosts) by investigating the network topology. For this, we used centrality, a measure of the connection amongst each host species (humans and domestic animals) in the network. A central host (i.e. high value of centrality) is the one that is infected by many parasites/pathogens that infect many other hosts in the network. Following Gómez et al. (2013), we assumed that the centrality of a given host species is a good estimate of its potential to be a source of parasites/pathogens to other species (domestic animals or humans). We hypothesized that a domestic host will be central in the network, i.e. it has a high value of centrality, if it was domesticated for a long enough time to have increased opportunities to share parasites/pathogens with humans but also with other domesticated animals.

2. Materials and methods

2.1. Sources of data

Data on parasites shared between humans and domesticated animals are from a book published by Ashford and Crewe (1998); those on shared infectious diseases are from McNeill (1976). We obtained a third source of more recent data using the Global Infectious Diseases and Epidemiology Network (GIDEON) database (www.gideononline.com). GIDEON is a medical database that provides continually updated data on the regional presence and epidemic status of pathogens and it has been used in various recent studies (Fincher et al., 2008).

Data on the total number of parasites and pathogens recorded in domestic animals were obtained from the EID2 database (www.zoonosis.ac.uk/EID2) (McIntyre et al., 2014). The EID2 systematically collates information on pathogens into a single resource using evidence from the NCBI Taxonomy database, the NCBI Nucleotide database, the NCBI MeSH (Medical Subject Headings) library and PubMed. Information about pathogens is assigned using data-mining of meta-data and semi-automated literature searches together with the total number of publications, which gives an estimation of the research effort to screen parasites. The total number of parasites/microbes was obtained by searching the number of parasites and microbes reported in each mammal species, and the total number of publications that referred to the association of each of microbe/parasite with each mammal species in consideration. The number of publications is then a proxy of the research effort on microbe/parasite diversity.

2.2. Statistical analysis and control for phylogenetic inertia and research effort

We first performed linear regressions on raw values of parasites/pathogens/diseases shared between domesticated animals and time to domestication from the three sources of data (McNeill, Ashford & Crewe, GIDEON).

Using information on mammal phylogeny (Binida-Emonds et al., 2007), we calculated the independent contrasts for each of the variables investigated with the package APE (Paradis et al., 2004) implemented in R (R Development Core Team 2012). To confirm the proper standardization of contrasts, we regressed the absolute values of standardized contrasts against their standard deviations. Contrasts were then analyzed using standard multiple regressions, with all intercepts forced through the origin. These variables were normalized using log transformation if needed. We then performed multiple linear regression on the independent contrasts (IC) of parasites/pathogens/diseases shared between domesticated animals on the four sources of data, including the EID2. To address the problem of sampling effort, we included the number of publications (obtained from www.zoonosis.ac.uk/EID2) as a covariate.

2.3. Network analysis

We used bipartite networks where nodes from hosts are interacting with nodes of pathogens/parasites, using the datasets of Ashford & Crewe and GIDEON. We projected these bipartite networks to unipartite networks using the 'tnet' package in R. These unipartite networks will represent patterns of relative interactions amongst domestic animals and humans through the occurrence of parasites/pathogens shared. Each host within a network plays a different role in pathogen sharing relative to all other nodes in the network. The role of each host within the network was examined using its centrality measurement. A central node (host) is the one that is highly connected to other nodes (hosts) and thus which is supposed to have a greater transmission potential of parasites/pathogens. We calculated the eigenvalue centrality (EC) with the 'evcent' function from the igraph package (Csardi and Nepusz, 2006) in R and we regressed the EC values to time to domestication.

3. Results

3.1. Relationships between shared parasites/pathogens and time since domestication

All three data sets showed no correlation between shared parasites/microbes/diseases and the total number of parasites/microbes/diseases identified using the EID2 (McNeill *vs* EID2, $P = 0.49$; Ashford & Crewe *vs* EID2, $P = 0.38$; GIDEON *vs* EID2, $P = 0.95$).

Research effort seemed to only slightly affect the number of diseases obtained from McNeill ($P = 0.07$), which may be explained by the use of old epidemiological sources of parasites/pathogens in this historical book. The number of parasites/pathogens shared between humans and parasites used in McNeill (1976) is affected by investigation effort, suggesting that an increase in investigation is necessary to give an accurate estimation of parasites/pathogens shared; this is also the case when using the more recent datasets (i.e., Ashford & Crewe and GIDEON).

Using several independent sources of data for parasites and infectious diseases and for domestication time (Table 1), we found positive relationships between the numbers of parasites and/or infectious diseases shared between humans and their domesticated animals and the length of time since their domestication (all $P < 0.05$, Fig. 1). Moreover, adding or removing rats from the datasets of Ashford & Crewe and GIDEON did not change the observed relationships.